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COMMENTS:

Re: U.S. Application No.: 09/731,255
Filed: December 6, 2000
Inventors: Habener, et al.
Entitled: Stem Cells and Their Use in Transplantation

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Habener et al.

Examiner: Bunner, B.E.

Serial No.: 09/731,255

Group: 1647

Filed: December 6, 2000

Entitled: Stem Cells and Their Use in
Transplantation

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SUPPLEMENTAL RESPONSE TO OFFICE ACTION

This paper is supplemental to Applicants' April 4, 2003 response to the Office Action dated December 4, 2002.

REMARKS

Applicants assert that the reference cited below provides additional support for the enablement of claims 25-35 and 67-79 of the instant application.

Rejection of Claims 25-35 and 67-79 Under 35 U.S.C. §112, first paragraph

Claims 25-35 and 67-79 are rejected under 35 U.S.C. §112, first paragraph for alleged lack of adequate written description and enablement.

In the Office Action dated December 4, 2002, the Examiner states that (1) "the specification does not teach transferring the pseudo-islet aggregates into any patient, especially to

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treat diabetes mellitus," (2) "[t]he specification does not teach that the transplanted pseudo-islet like aggregates act like healthy islet cells," and (3) "[s]ince claim 25 recites that the patient does not serve as the donor for the nestin-positive pancreatic stem cells, the skilled artisan cannot predict that the differentiated pseudo-islet like aggregates can be successfully immunologically transplanted into the recipient patient."

Applicants assert that in view of Applicants' response to the December 4, 2002 Office Action, filed on April 4, 2003, claims 25-35 and 67-79 are fully enabled. The reference cited below provides additional support for enablement of claims 25-35 and 67-79 of the instant application.

It is well established that post-filing documentation or publications may be used to demonstrate that Applicants disclosure was enabling at the time of filing (*See, e.g., In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995)). Accordingly, Applicants submit herewith, Exhibit A which demonstrates that the methods disclosed by Applicants in the present application were sufficient to enable one of skill in the art to practice the claimed method of treating a patient with diabetes mellitus as of the filing date.

Applicants submit that there is post-filing date literature teaching treatment of diabetic NOD-SCID mice by implantation of islet-like cell clusters (ICCs) derived from cultured human fetal nestin-positive islet-derived progenitor cells. (See Exhibit A, Huang and Tang, "Phenotype Determination and Characterization of Nestin-positive Precursors Derived from Human Fetal Pancreas," *Laboratory Investigation*, 83(4): 539-547 (2003)).

This publication demonstrates the actual reduction to practice of the invention of the instant application, as claimed in independent claims 25 and 67. "Pseudo-islet like aggregates" are defined in the application at page 13, lines 17-21. Applicants submit that one of skill in the art would accept that the nestin positive ICCs described in Exhibit A are equivalent to the "pseudo-islet like" aggregates of the instant application. That is, the nestin positive ICCs of Exhibit A are "artificial aggregates of insulin-secreting cells which resemble in form and function the islets of Langerhans of the pancreas", as described in the instant application at page 13, lines 17-21; page 29, lines 17-24; and Examples 2 and 3.

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The data presented in Huang et al. (Exhibit A) demonstrate the treatment of diabetes mellitus by the transfer of ICCs into a patient. Exhibit A teaches that 500 ICCs were introduced to each mouse; a dosage consistent with that taught by the present specification.

Exhibit A demonstrates that, in contrast to the Examiner's assertion, the transplanted pseudo-islet like aggregates (ICCs) act like healthy islet cells and effect blood glucose levels, resulting in reversal of hyperglycemia, indicative of diabetes treatment.

Exhibit A demonstrates the successful implantation of human nestin-positive cell aggregates into mice. That is, data presented in Exhibit A demonstrate that diabetes can be treated, as indicated by a reversal of hyperglycemia, without the occurrence of transplant rejection or graft rejection, even if the patient is not the donor for the nestin-positive aggregates. Thus, in view of the teachings of the specification, in further view of this publication and the abstracts of Wu, presented in Exhibits A and B in Applicants April 4, 2003 response to the December 4, 2002 Office Action, one of skill in the art would have no reason to predict that graft or transplant rejection would occur if a human patient were transplanted with pseudo-like aggregates derived from any of the following: another human, a pig, monkey rat, etc... Thus, Applicants submit that where the methods described in Exhibit A, presented herewith, as well as Exhibits A and B presented with Applicants' April 4, 2003 response, essentially mirror the teaching of the present specification, one of skill in the art would have been able to reproduce the claimed invention as of the filing date, without undue experimentation.

Although, the studies performed in Exhibit A, presented herewith, and Exhibits A and B presented with Applicants' April 4, 2003 response were conducted in an art recognized animal model of diabetes, Applicants submit that *In re Brana* also provides that such *in vivo* animal testing is sufficient to meet the patentability requirements for an invention relating to the treatment of humans. *Id.*

In view of the above, and further in view of Applicants' April 4, 2003 response to the December 4, 2002 Office Action, Applicants submit that claims 25-35 and 67-79 meet the legal requirements for enablement and respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph rejection.

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CONCLUSION

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Date: May 22, 2003

Respectfully submitted,



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